COLLEGE of AMERICAN PATHOLOGISTS

Educational Discussion: Accuracy Based Testosterone and Estradiol

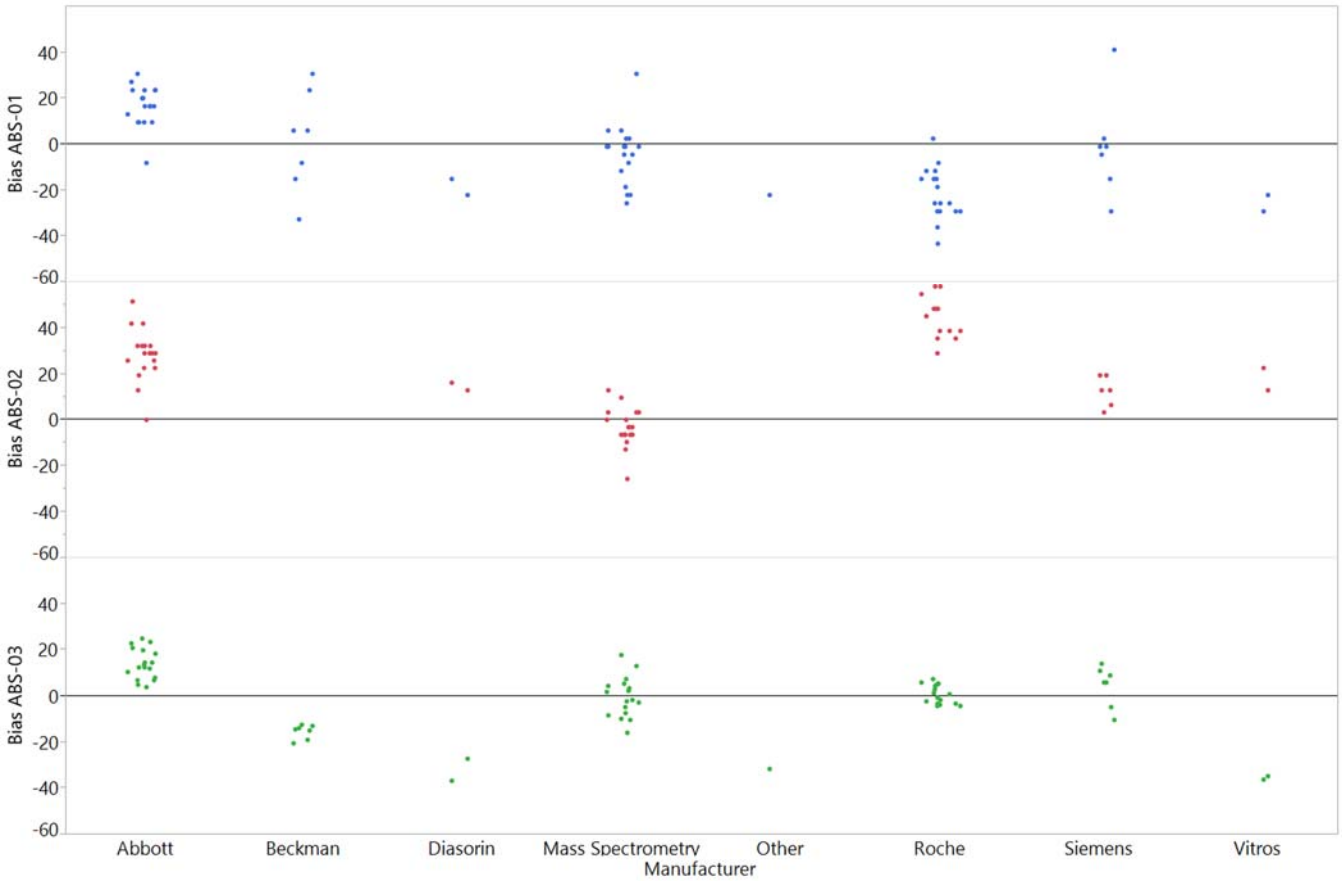
This ABS Survey, as well as all accuracy-based Surveys, use specimens processed in a manner that minimize matrix effects and thus are, with regards to the material characteristics, as similar as possible to regular patient specimens. Because the specimens used in this Survey can be considered a patient specimen, this Survey provides information about the possible variability in measurement results of a patient sample measured by different assays and laboratories.
Table 1 provides a summary of individual results reported for each sample and analyte. The data suggest that for most samples the frequency distributions of reported results are normal and therefore the coefficient of variation (%CV) provides an appropriate description of the extent of variability in measurement results.
Analytes with high variability in measurement results (%CV ≥20%) are estradiol, testosterone and SHBG. The high variability in sample ABS-02 for SHBG is caused by an outlier from an undefined assay. When this outlier is removed, the variability is 13.2 %CV.

Table 1: Summary of measurement results by sample and analyte (for measurement units see detailed PSR tables)

Analyte	Sample	Min/Max	Median	Mean	%CV
Albumin	ABS-01	3.7/4.4	3.9	3.9	3.8
	ABS-02	3.6/4.4	4.1	4.0	4.8
	ABS-03	3.2/4.2	3.9	3.9	6.1
Calcium	ABS-01	8.3/9.1	8.8	8.7	2.1
	ABS-02	8.6/9.9	9.1	9.1	2.4
	ABS-03	8.3/9.2	8.8	8.8	2.4
Cortisol	ABS-01	9.2/14	11.0	11.1	8.1
	ABS-02	8.2/11.6	9.2	9.3	7.6
	ABS-03	8.3/16.4	9.6	9.8	13.2
Estradiol*	ABS-01	5/57	12.0	13.7	**68.0**
	ABS-02	29/166	54.0	56.3	**30.7**
	ABS-03	10/48	27.0	28.3	**22.9**
FSH	ABS-01	40.2/55.4	46.7	46.7	8.5
	ABS-02	4.4/7.2	5.4	5.5	12.7
	ABS-03	13.7/20.4	16.4	16.6	10.2
LH	ABS-01	18.5/31.2	25.8	25.8	16.3
	ABS-02	6.7/11.6	10.2	9.3	17.7
	ABS-03	8/14.7	11.9	11.9	17.7
SHBG	ABS-01	14.2/27.56	23.6	23.1	12.9
	ABS-02	3.2/31	25.3	24.6	**20.9**
	ABS-03	11.7/55.22	44.8	44.0	16.9
Testosterone	ABS-01	16/40	27.0	27.3	**20.2**
	ABS-02	23/452	40.0	46.2	**106.5**
	ABS-03	123/244	201.0	195.8	13.8
TSH	ABS-01	1.84/3.09	2.3	2.4	15.5
	ABS-02	1.02/1.61	1.2	1.2	9.8
	ABS-03	1.91/3.12	2.3	2.5	14.6

*The statistical analysis represent data after outlier removal
The high variability in measurement results for testosterone in samples ABS-01 (target value: 28.4 ng/dL) and ABS-02 (target value: 31.1 ng/dL) can be explained with systematic differences among manufacturers with mean bias, calculated from all results on all 3 samples, ranging between -14.9% for Vitros systems to 29.3% for Beckman systems. The high %CV in ABS-02 of 106.5% listed in table 1 is mainly -caused by an outlier result from an unspecified assay. However, even with the outlier removed the variability is still 25 %CV. The variability in sample ABS-03 (target value: 196 ng/dL) is much lower then for the other samples. The increase in measurement bias with decreasing analyte concentration suggests that the bias is mainly -caused by interferring substances. Assuming that each assay manufacturer uses a different antibody with different crossreactivites towards other compounds would explain the high systematic differences among assay manufacturers. Mass spectrometry assays show a high level of accuracy that does not seem to be affected by interferring compounds. Among the immunoassays, the Siemens systems show the lowest mean bias (7.81%). The Siemens system are the only immunoassays standardized by the CDC Hormones Standardization Program at the time this survey was conducted.

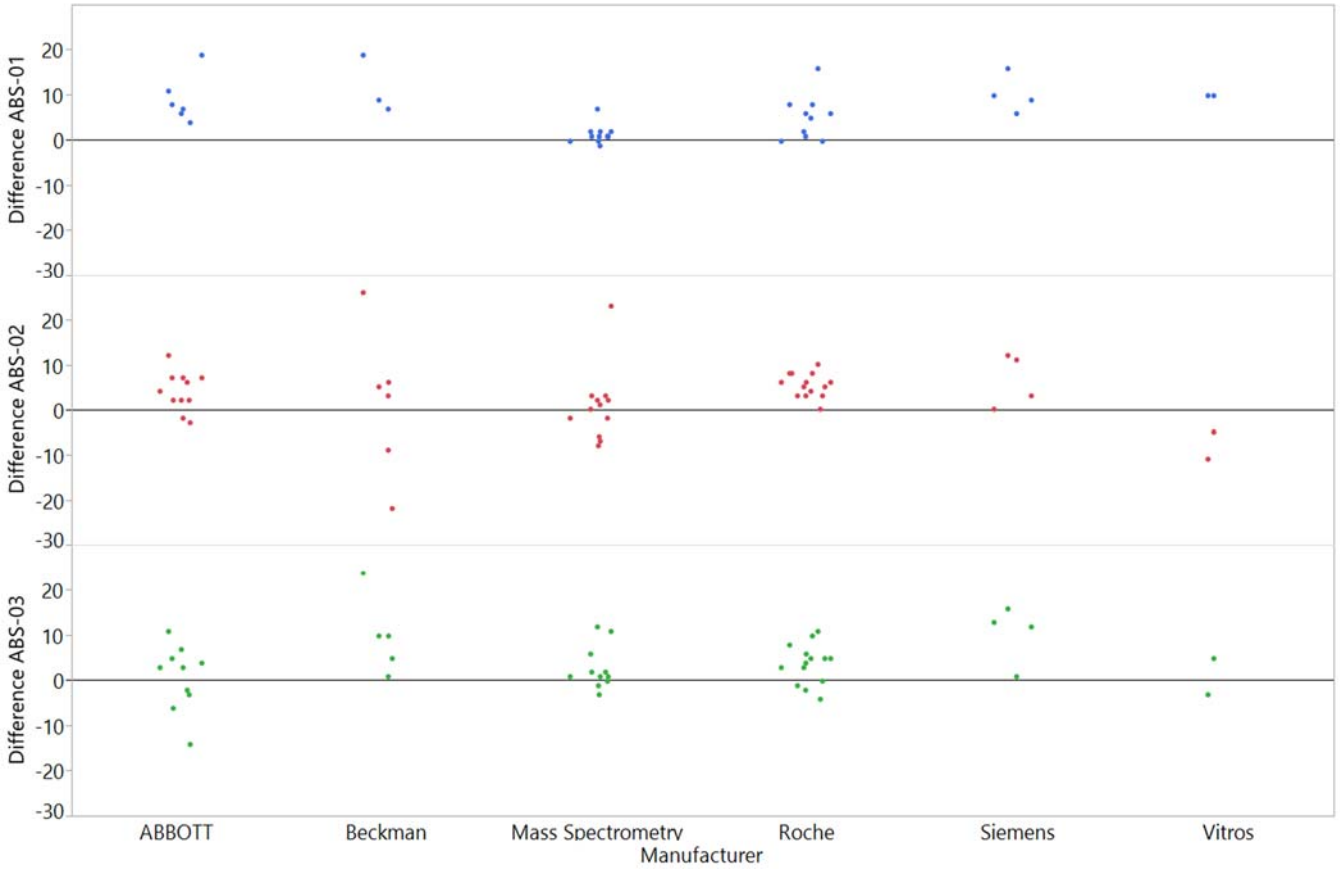
Figure 1: Bias distribution of individual reported results by assay manufacturer



The variability in estradiol measurements appears more consistent among assay manufactures than for testosterone measurements with assays showing mainly a positive bias in all samples with a mean bias ranging from 10.2 % for mass spectrometry assays to 72% for Siemens assays. The target value for sample ABS-01 is 6.24 pg/mL. Therefore, the actual difference to the target value

would be a more descriptive parameter than the percent bias. The mean difference between the measured values and the target value in this sample ranged between 1.21 pg/mL for mass spectrometry assays and 11.4 pg/mL for the Beckman assay.
It has been suggested that treatment of women with aromatase inhibitor therapy for breast cancer is successful when estradiol levels are suppressed to less than 9.9 pg/mL. Of the 38 results reported for sample ABS-01 (target value 6.24 pg/mL), 23 results (60%) were greater than 10 pg/mL. Of the 15 results below 10 pg/mL, 10 results were reported from mass spectrometry assays. These findings suggest that immunoassays have a high likelihood of not correctly assessing the success of aromatase inhibitor therapy in women with breast cancer than mass spectrometry assays.

Figure 2: Bias distribution of individual reported results by assay manufacturer *



* Bias for sample ABS-01 is expressed as difference between the measured value and the target value in pg/mL. For ABS-02 and ABS-03 the bias is expressed as difference between the measured value and target value in percent.

Hubert W. Vesper, PhD
Accuracy-Based Programs Committee